In the claims

Please cancel claims 5-19, 23-29, 34-49, and 42-47.

Remarks

Applicants have cancelled claims solely for the purpose of reducing the filing fees. No new matter has been added.

Applicants have amended the specification to provide priority application information and information regarding the publication in English under PCT Article 21(2) of the PCT application of which the above-identified application is a U.S. national stage application. No new matter has been added.

Respectfully submitted,

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Attorney Docket No.: B0192/7029 ERP
Dated: 8 June 2001
x06/10/01x

Added Section:

This application is a national stage filing 35 U.S.C. §120 or 35 U.S.C. §365(c) of PCT International application PCT/GB99/04182 designating the United States of America, and filed December 10, 1999, of which this application is a national stage filing under 35 U.S.C. §371, was published under PCT Article 21(2) in English.

Foreign priority benefits are claimed under 35 U.S.C. §119(a)-(d) or 35 U.S.C. §365(b) of British application number 9827228.9 filed December 10, 1998, which designated at least one country other than the United States.

International Preliminary Examining Authority
EUROPEAN PATENT OFFICE,
Erhardtstrasse 27,
D-80331 MUNICH,
GERMANY.

8 December 2000

Dear Sirs,

International Patent Application No. PCT/GB00/04182
THE UNIVERSITY OF NOTTINGHAM et al
Representative's Ref: SCB/51598/001

I am writing in response to the Written Opinion dated 9 August 2000 issued in respect of the above-referenced International Patent Application.

On behalf of the Applicants I would like to make the following comments on various points raised by the Examiner in the Written Opinion:

Independent claims 1 and 48

The Examiner is of the opinion that claims 1 and 48 lack novelty in view of document D1.

The present inventors are all named as authors of the abstract cited as document D1 and they respectfully submit that the Examiner has mis-interpreted the disclosure of this abstract. D1 actually describes use of MUC1 antigen preparations to detect the presence of anti-MUC1 autoantibodies in a sample of bodily fluid (a serum sample). The MUC1 antigen preparation may be normal urinary MUC1 protein, tumour-associated MUC1 protein or a synthetic MUC1 peptide. Thus, in D1 the serum sample is contacted with a preparation of MUC1 protein or peptides in order to detect the presence of auto-antibodies in the serum. This is (immunologically) the opposite of the method of claim 1. The method of claim 1 is based on the use of autoantibodies to detect the presence of a cancer-associated antigen in samples of bodily fluid. Thus, claim 1 clearly relates to a method in which a sample of bodily fluid is contacted with auto-antibodies in order to detect the presence of antigen within the sample.

Just because a particular protein or peptide antigen is capable of detecting antibodies of a certain specificity in a serum sample it does not follow that if the antibodies were isolated and then used as a reagent they would be capable of specifically detecting the presence of the antigen in a sample

containing a multitude of different antigens. The present inventors are the first to show, surprisingly, that autoantibodies having specificity for cancer-associated antigens can be isolated from serum and then in turn used to detect the presence of the cancer-associated antigen in a sample of bodily fluid, for example serum.

In summary, none of the prior art cited by the Examiner discloses or even suggests that it is possible to purify/isolate circulating autoantibodies reactive with cancer-associated antigens which may then be used as a reagent to detect the presence of cancer-associated antigens in a sample from a patient. Accordingly, the methods of claims 1 and 48 and the claims dependent thereon are novel and inventive in view of the cited prior art.

Independent claims 20 and 50

The Examiner is of the opinion that document D1 discloses a reagent which comprises mammalian autoantibodies with a specificity for one epitope of a mammalian cancer-associated marker protein.

As explained above, the 'reagent' used in D1 is actually a MUC1 antigen preparation, for example normal urinary MUC1 protein, tumour-associated MUC1 protein or a synthetic MUC1 peptide. It is this MUC1 antigen preparation which is added to a serum sample in order to detect the presence of auto-antibodies within the sample. There is no disclosure in D1 of a diagnostic reagent containing isolated or purified autoantibodies, nor any suggestion that circulating autoantibodies could be used as the basis of a diagnostic reagent. Accordingly, claim 20 and the claims dependent thereon are both novel and inventive in view of document D1.

Independent claims 30 and 50

The Examiner is of the opinion that claims 30 and 50 lack inventive step in view of document D1.

As aforesaid, document D1 actually discloses the use of a MUC1 antigen preparation to detect the presence of anti-MUC1 autoantibodies in serum samples taken from normal individuals or advanc d breast cancer patients. D1 certainly does not disclose or even suggest that circulating auto-antibodies to a cancer-associated marker can themselves be used to detect the presence of cancer-associated marker proteins in a sample from a patient.

In the absence of any teaching relating to the use of autoantibodies to detect the presence of cancer-associated marker proteins in a sample from a patient there is nothing in document D1, or indeed in any of the prior art cited by the Examiner, which would lead the skilled artisan to attempt to use auto-antibodies in this way or to prepare immortalized cell populations capable of producing autoantibodies having specificity for cancer-associated marker proteins. Accordingly, claims 30 and 50 and the claims dependent thereon are inventive in view of document D1.

Independent claims 40 and 49

The Examiner is of the opinion that claims 40 and 49 also lack inventive step in view of document D1.

The comments set forth above regarding the disclosures of document D1 apply equally to this objection. D1 quite simply fails to disclose a method in which autoantibodies are used to detect the presence of cancer-associated marker proteins in a sample of bodily fluid. As such, it would not be obvious in the light of the disclosure of D1 to provide a kit comprising mammalian autoantibodies for use in detecting the presence of a cancer-associated marker protein in a bodily fluid of a mammal. Claims 40 and 49 and the claims dependent thereon are therefore inventive in view of document D1.

Claims to immortalized cell populations

With regard to the Examiners comments on the immortalized cell population of claims 30-39 and 51 set forth in paragraph 1 of Item VIII, the skilled artisan will recognise that these claims relate in general to immortalized cell populations having the characteristics of *"producing autoantibodies directed against at least one epitope of a mammalian cancer-associated marker protein"* and not to any particular cell population. The description provided in the application as filed of how to make an immortalized c ll population according to these claims is sufficiently clear and complete to enable a skilled reader to reproduce the invention without undue burden. It is therefore submitted that there is no need for reference to a microorganism deposit to support these claims.

Clarity objections

The applicants note the Examiner's comments on the clarity of the claims set forth in paragraphs 2 to 4 of Item VIII, however, it is preferred to address these objections in the National Phase.

Favourable reconsideration of this application in the light of the comments set out above is respectfully requested.

Please acknowledge safe receipt of this letter by stamping and returning the enclosed EPO Form 1037.

Yours faithfully,

BALDOCK; Sharon Claire
Authorised Representative

Enclosure